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SCIENTIFIC INVESTIGATIONS

Differences in sleep measures and waking electroencephalography of patients with insomnia according to age and sex

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Study Objectives: Sleep characteristics are known to be different according to age and sex. The objective of this study was to investigate differences in sleep parameters and quantitative electroencephalography of patients with insomnia according to age and sex.

Methods: Patients with insomnia disorder ages 40–79 years were recruited. Each participant was assessed with the Pittsburgh Sleep Quality Index, 4-day wrist actigraphy, and quantitative electroencephalography derived from a 64-channel electroencephalogram system. These variables were compared between age groups (40–64 years vs 65–79 years) and sexes.

Results: Among 173 participants, 61 (35%) were ages 65–79 years and 64 (35%) were males. The older group reported shorter (P = .009) total sleep time than the middle-aged group based on the Pittsburgh Sleep Quality Index, while women slept longer than men based on actigraphy (P = .040). Regarding electroencephalography, women had higher relative beta power than men (P = .006). Older patients showed slower dominant occipital frequency than younger patients (P = .008). The age effect was more noticeable on both clinical variables and quantitative electroencephalography for women. Compared with younger women, older women reported shorter total sleep time in the Pittsburgh Sleep Quality Index (P = .025), underestimated their sleep time (Pittsburgh Sleep Quality Index total sleep time/actigraphic total sleep time, P = .034), and showed reduced alpha power in the frontal area (P = .009).

Conclusions: Clinicians should be aware of the age and sex difference on manifestation of insomnia, which may further impact an individual's behaviors, such as staying in bed for a longer time or seeking sleep aids.

Keywords: actigraphy, age, electroencephalography, insomnia disorder, sex

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Insomnia disorder, characterized by hyperarousal, is more prevalent in women than in men, and sleep disturbance increases with age. Age and sex differences of clinical manifestation and neurophysiologic changes in insomnia disorder have been hypothesized, but not thoroughly investigated.

Study Impact: Our data showed that women with insomnia were not specifically more vulnerable to objective sleep disturbances but were more prone to a self-reported sense of sleep disturbances. The brain activity examined by electroencephalography showed a sex difference in insomnia. Women's predisposition to hyperarousal may lead to a higher incidence of insomnia and their greater engagement in compensatory behaviors. There were age-related phenomena as well, particularly affecting older women.

INTRODUCTION

Manifestation and impact of sleep and its disturbances differ with age and sex. A number of studies, including meta-analyses, have consistently shown that total sleep time (TST), sleep efficiency, and percentage of slow-wave sleep are decreased, while sleep latency and wake after sleep onset (WASO) are increased with age.[1,2] The nature of sleep also differs between men and women. In general, women report poorer sleep quality, longer sleep onset latency, frequent night awakenings, and longer time awake after sleep onset compared with men.[3,4] However, objective data by polysomnography and actigraphy show that women have better sleep with longer TST and a greater percentage of slow-wave sleep than age-matched men.[1] Aging effects and sex differences in normal sleep might underlie differences in risks and characteristics of sleep disorders.

Insomnia disorder, characterized by significant complaint of dissatisfaction with sleep quality or quantity, is one of the most prevalent sleep disorders. According to several epidemiologic studies, sleep disturbances increase with age, and female predominance in the prevalence of insomnia has been consistently reported.[5–8] Further, use of sleep aid is also higher in women than men and increases with age.[9–11] Therefore, age and sex differences might exist in the pathophysiology of insomnia, its clinical manifestations, and attitude and tolerance of patients to insomnia. However, studies investigating age and sex differences in manifestations of insomnia disorder are limited. Pillai et al[12] have found that difficulties in sleep induction are more common in younger adults, while sleep maintenance is the most

frequently reported problem in middle-aged and older adults. Another study on older adults with insomnia has also confirmed the difficulty of sleep maintenance as the most prevalent symptom among older patients.[13] In addition, older women tend to experience more difficulty initiating sleep and have multiple insomnia symptoms than older men, indicating that there are also sex differences of insomnia.[13]

Differences in electroencephalography (EEG) according to age and sex are also expected in insomnia since hyperarousal is a key feature of insomnia evidenced by EEG activity.[14,15] In general, patients with insomnia have elevated levels of high-frequency and reduced slow-frequency EEG activity during sleep onset period and sleep time, opposite to those of normal sleepers.[16–20] Moreover, increased power of high-frequency EEG activity during sleep has been observed to be more prominent in women than in men with insomnia, suggesting sex differences.[21,22] Evaluating patients with insomnia during wake has become increasingly important as fatigue and impaired function during daytime cause great distress to patients with insomnia. Studies of daytime EEG in insomnia have also revealed increased high-frequency power, indicating that hyperarousal is not limited to night sleep.[23,24]

To the best of our knowledge, age and sex differences in clinical manifestations of insomnia and associated neurophysiologic findings using resting-state EEG have not been reported. Thus, the objective of this study was to determine differences in sleep parameters (self-reported and objective) and neurophysiologic findings (based on EEG) of patients with insomnia according to age (middle-aged vs older adults) and sex (male vs female). The possible interaction between age and sex was also examined for both clinical and EEG parameters. We hypothesized that (1) older patients might experience a more severe degree of insomnia symptoms compared with their younger counterparts, (2) female patients tend to overestimate their insomnia symptoms, and (3) both age and sex difference might be attributed to their different brain activity, probably associated with hyperarousal or regional dysfunction.

METHODS

Participants

A total of 173 patients with chronic insomnia disorder who visited Seoul National University Bundang Hospital from September 2017 to December 2019 were enrolled for this study. Inclusion criteria were as follows: (1) individuals aged 40 to 80 years, (2) those who were diagnosed with insomnia disorder based on the *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition, and (3) those who had not undergone any treatment for insomnia including medication and cognitive-behavioral therapy for 1 year. Patients with major mental illness (eg, schizophrenia, bipolar disorder, severe major depressive disorder with significant suicidal ideation, and other types of psychotic disorders), significant medical or neurologic conditions, or other sleep disorders (eg, sleep apnea, restless legs syndrome, and periodic limb movement disorder) were excluded. All participants underwent an interview with psychiatrists to confirm their diagnoses and polysomnography to detect and exclude sleep apnea (apnea-hypopnea index ≥ 15 events/h) and other sleep disorders. Patients were divided into a middle-aged group (< 65 years old) and an older adult group (≥ 65 years old) to compare sleep characteristics by age. All participants were informed of the purpose and procedures of this study. They provided written informed consent before participating in this study. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB no. E-1705-396-001).

Questionnaires

Sleep questionnaires included the Insomnia Severity Index for insomnia severity, the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and the Epworth Sleepiness Scale for daytime sleepiness. Anxiety and depression were also assessed using the Beck Depression Inventory II and the Beck Anxiety Inventory. To assess how participants perceived their habitual sleep, sleep parameters derived from the PSQI were used. Participants reported their usual bedtime and rise time, from which time in bed (TIB) was calculated. Sleep onset latency and TST were also reported. Sleep efficiency (SE) was calculated by dividing TST by TIB.

Actigraphy

Participants were required to wear a triaxial accelerometer (wGT3x-BT; ActiGraph LLC, Pensacola, FL) on their nondominant wrist for 4 consecutive days. Only data from participants whose compliance rates exceeded 75% (at least 3 out of 4 nights) were used for analysis. During the period of actigraphic recordings, individuals kept a daily sleep diary of bedtime and rise time. The wGT3x-BT estimated sleep–wake status by capturing and recording physical activity. The Cole-Kripke algorithm was adopted to calculate the following 4 sleep parameters (TST, sleep onset latency, SE, and WASO) using ActiLife 6 software (ActiGraph LLC). All parameters were calculated as daily averages for each participant. To assess the congruence between self-perceived habitual sleep time and actigraphy-measured sleep time, the ratio of sleep time (dividing PSQI-derived TST by actigraphic TST) was calculated as described previously.[25] By using ratio scores that combined TST from 2 different assessments, the degree of sleep time misperception, either under- or overperception of sleep, was identified.

Quantitative EEG

Waking EEG was recorded in a sitting position for 15 minutes. Participants were instructed to close their eyes and relax but to stay awake. Electrodes were placed according to the extended international 10–20 system. EEG signals were amplified and digitalized with a 64-channel Neuroscan Synamps (Compumedics, Charlotte, NC) at a sampling rate of 1 kHz. EEG data were processed using Neuroguide (NeuroGuide; Applied Neuroscience, Inc., St. Petersburg, FL). A high-pass filter was set to be 100 Hz, with a low-pass filter set to be 0.3 Hz. Each electroencephalogram was visually inspected to exclude artifacts caused by muscle activity, small body movements, eyelid movements, and microsleep. An artifact-free 90-second EEG recording was

selected. Spectral analysis was then performed with fast Fourier transform to compute absolute and relative power values of 4 bands (delta: 1.0–4.0 Hz; theta: 4.0–8.0 Hz; alpha: 8.0–12.0 Hz; and beta: 12.0–25.0 Hz). Relative power values (percentages of power of each band in total power) were used in this study to minimize interindividual variance and facilitate comparisons by age and sex. Electrodes were grouped into 5 cerebral regions: frontal (FP1, FP2, F3, F4, F7, and F8), temporal (T3, T4, T5, and T6), central (C3 and C4), parietal (P3 and P4), and occipital (O1 and O2). Relative power was calculated as the mean value for each region. Dominant occipital frequency (DOF) was computed by averaging the peak frequency of 2 occipital electrodes.

Statistical analysis

Comparisons of demographics, clinical variables, and EEG power by age and sex were performed using independent *t* test or χ^2 test. To compare variables with covariates adjusted, analysis of covariance was performed. Two-way analysis of covariance was also conducted to test group by sex interaction effects. Between-group comparisons of regional distribution in each EEG band were performed using a generalized estimating equation.[26] All significance tests were 2-sided and *P* values < .05 were considered statistically significant. IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY) was used for all statistical analyses.

RESULTS

Among 173 patients with insomnia disorder, 64 (35.3%) were males and 61 (35.3%) were ages 65 years or older. According to polysomnography, their mean TST, sleep onset latency, SE, WASO, and apnea-hypopnea index were 352.54 ± 57.51 minutes, 26.49 ± 30.65 minutes, 72.51% ± 12.75%, 106.42 ± 53.07 minutes, and 5.34 ± 4.35 events/h, respectively. After excluding 16 patients who failed to wear the actigraph for at least 3 days, valid actigraphic data were collected from 157 (90.8%) patients, yielding a total of 621 nights.

Clinical sleep parameters

Table 1 shows demographic and clinical data of the 2 age groups with sex adjusted as a covariate. The mean PSQI total score was higher in the older adult group than that in the middle-aged group (middle-aged vs older adults: 11.85 ± 2.75 vs 12.74 ± 2.43; *P* = .022). Older adult patients reported significantly shorter TST (middle-aged vs older adults: 253.53 ± 70.18 minutes vs 219.85 ± 77.79 minutes; *P* = .008) and lower SE (middle-aged vs older adults: 67.71% ± 20.99% vs 59.01 ± 20.94%; *P* = .009) in the PSQI. A similar tendency of older patients having more disturbed sleep was observed in actigraphy as well (TST, SE, WASO). However, none of the variables reached statistical significance.

Table 1—Comparison of demographic and clinical data between age groups.

	Middle-Aged (n = 112)	Older Adult (n = 61)	*P*
Age, y	54.74 (6.63)	69.69 (4.00)	< .001***
Male, n (%)	35 (31.3)	29 (47.5)	.034*
BMI, kg/m^2	22.73 (2.64)	22.70 (2.49)	.944
Questionnaire			
PSQI, score	11.85 (2.75)	12.74 (2.43)	.022*
TIB, min	391.61 (99.89)	387.70 (104.49)	.976
TST, min	253.53 (70.18)	219.84 (77.79)	.008**
SE, %	67.71 (20.99)	59.01 (20.94)	.009**
SOL, min	74.25 (59.10)	83.03 (59.08)	.230
ISI, score	18.20 (5.42)	18.05 (4.67)	.807
ESS, score	8.43 (5.11)	7.20 (4.87)	.123
BDI-II, score	14.83 (8.39)	17.89 (10.58)	.055
BAI, score	11.25 (8.66)	12.54 (10.46)	.330
Actigraphy (n = 157)	(n = 101)	(n = 56)	
TIB, min	419.39 (79.96)	408.35 (85.32)	.621
TST, min	344.07 (65.68)	325.04 (73.40)	.185
SE, %	82.47 (7.96)	79.71 (8.53)	.063
SOL, min	6.06 (7.81)	5.89 (5.89)	.838
WASO, min	69.26 (38.15)	77.42 (39.17)	.185
Ratio of TST, %	75.95 (23.08)	71.70 (32.35)	.293

Pearson's χ^2 test was performed for differences between categorical variables and ANCOVA was used for differences between means. Sex was adjusted as a covariate. Data are presented as mean (standard deviation) unless otherwise indicated. *P < .05, **P < .01, ***P < .001. ANCOVA = analysis of covariance, BMI = body mass index, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory II, ESS = Epworth Sleepiness Scale, ISI = Insomnia Severity Index, PSQI = Pittsburgh Sleep Quality Index, SE = sleep efficiency, SOL = sleep onset latency, TIB = time in bed, TST = total sleep time, WASO = wake after sleep onset.

There was no significant sex difference in the self-reported questionnaires regarding sleep, anxiety, or mood. In actigraphy, males with insomnia showed shorter TST than females (male vs female: 320.28 ± 79.82 minutes vs 346.97 ± 60.14 minutes; P = .040). The difference in other actigraphic parameters or the ratio of TST was not significant between males and females (**Table 2**).

There was no significant age group by sex interaction in self-reported sleep parameters, objective sleep parameters, or the ratio of TST. In subgroup analyses, age effect was only significant in women but not in men (**Table 3**). The aforementioned age group difference, the shorter PSQI TST in the older adult group compared with the middle-aged group, remained significant in the female group (P = .025). In addition, older adult women showed a lower ratio of TST (P = .034) and poorer actigraphic SE (P = .043) than middle-aged women. On the other hand, the sex difference was observed in both age groups. Women stayed in bed for a longer time than men in the older adult group (sleep diary TIB, P = .017) and in the middle-aged group (PSQI TIB, P = .032).

Quantitative EEG

EEG data were obtained from 170 (98%) participants. Results showed significant age group by region interaction in the relative power of the theta band (χ^2 = 10.02, P = .040). In posthoc analyses, we could not find a significant group difference of the theta band in a specific brain region. For other bands, there was no significant interaction or main group effect. Regarding the DOF, the older adult group showed a slower DOF than the middle-aged group (middle-aged vs older adults: 9.51 ± 0.38 vs 9.33 ± 0.41; P = .008).

Sex by region interaction was found to be significant in the delta (χ^2 = 13.93, P = .008), theta (χ^2 = 12.13, P = .016), and beta (χ^2 = 14.88, P = .005) bands. In the beta band, the main sex effect was also significant (χ^2 = 7.41, P = .006). The female group showed higher beta power in all 5 brain regions (frontal, P = .014; temporal, P = .049; central, P = .001; parietal, P = .012; occipital, P = .047) (**Figure 1**). For relative delta and theta power, there was no sex difference in a specific region. There was no significant difference in the DOF between sexes (P = .248).

The age group by sex interaction on EEG was also examined and was observed to be significant in the delta (χ^2 = 405.01, F = 4.66, P = .032) and alpha (χ^2 = 1022.34, F = 4.02, P = .047) bands in the frontal area (**Figure 2**). As shown in **Figure 2**, the age effect differed between men and women regarding the frontal delta and alpha power. In posthoc analysis, there was a significant decrease of frontal alpha power in older women compared with younger women (P = .009), whereas no significant difference was observed between younger and older men. The delta power did not significantly differ between age groups in both sexes. For the DOF, there was no significant interaction between age group and sex. The age effect, slowed DOF observed in the older adult group compared with their

Table 2—Comparison of demographic and clinical data between sexes.

	Males (n = 64)	Females (n = 109)	*P*
Age, y	61.80 (9.63)	58.96 (8.87)	.051
BMI, kg/m^2	23.35 (2.67)	22.35 (2.46)	.014*
Questionnaire			
PSQI, score	11.91 (2.60)	12.31 (2.70)	.156
TIB, min	373.28 (92.18)	400.19 (105.35)	.073
TST, min	230.39 (75.28)	248.26 (73.58)	.305
SE, %	64.63 (23.10)	64.65 (20.32)	.565
SOL, min	67.49 (58.18)	82.99 (59.09)	.095
ISI, score	18.34 (5.20)	18.03 (5.15)	.771
ESS, score	7.97 (5.29)	8.01 (4.92)	.885
BDI-II, score	16.89 (10.75)	15.53 (8.35)	.372
BAI, score	11.16 (11.53)	12.03 (7.78)	.618
Actigraphy (n = 157)	(n = 57)	(n = 100)	
TIB, min	397.54 (89.63)	425.65 (75.58)	.053
TST, min	320.28 (79.82)	346.97 (60.14)	.040*
SE, %	80.54 (8.78)	82.02 (7.92)	.464
SOL, min	6.27 (8.31)	5.85 (6.47)	.639
WASO, min	70.99 (35.87)	72.84 (40.22)	.567
Ratio of TST, %	76.04 (33.48)	73.52 (22.12)	.433

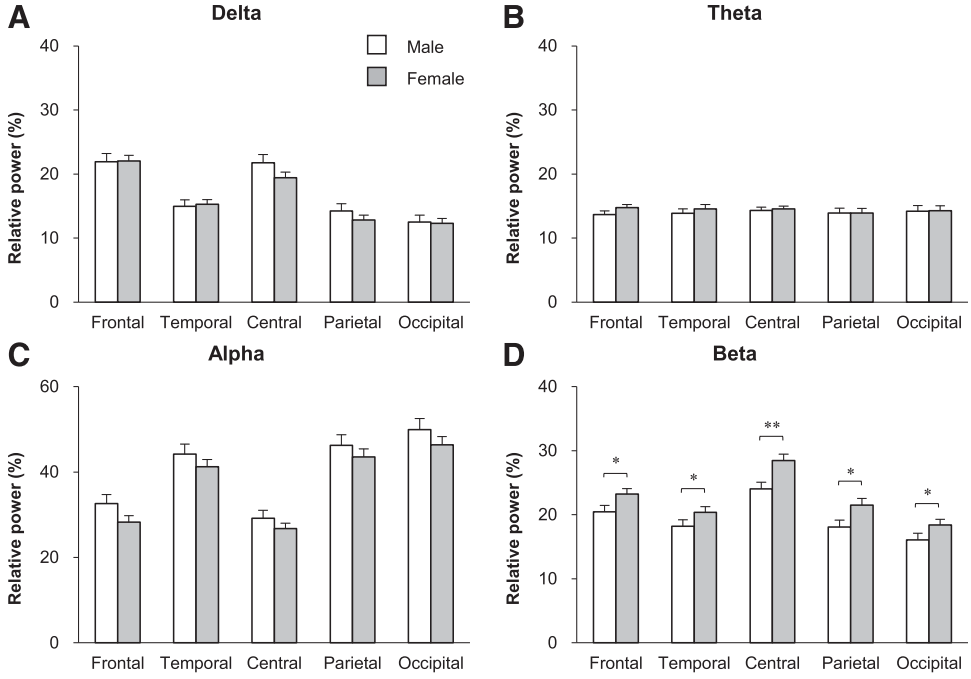
Pearson's χ^2 test was used for differences between categorical variables and ANCOVA was performed for differences between means. Age was adjusted as a covariate. Data are presented as mean (standard deviation). *P <.05. ANCOVA = analysis of covariance, BMI = body mass index, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory II, ESS = Epworth Sleepiness Scale, ISI = Insomnia Severity Index, PSQI = Pittsburgh Sleep Quality Index, SE = sleep efficiency, SOL = sleep onset latency, TIB = time in bed, TST = total sleep time, WASO = wake after sleep onset.

Table 3—Subgroup analyses of sleep parameters in men and women.

	Males			Females			*P*	
	Middle-Aged (n = 31)	Older Adult (n = 26)	*P*	Middle-Aged (n = 70)	Older Adult (n = 30)	*P*	Middle-Aged Males vs Females	Older Adult Males vs Females
TIB								
PSQI, min	363.88 (97.63)	378.08 (87.91)	.570	409.72 (97.43)	401.66 (119.60)	.725	.032*	.410
Sleep-log, min	412.74 (84.12)	379.42 (94.21)	.164	422.33 (78.50)	433.42 (68.94)	.504	.581	.017*
Ratio (PSQI:sleep-log), %	91.57 (30.78)	111.67 (77.00)	.301	98.11 (20.09)	92.96 (23.31)	.266	.207	.210
TST								
PSQI, min	235.65 (62.11)	214.62 (88.87)	.299	261.00 (72.11)	225.00 (72.53)	.025*	.093	.632
Actigraphy, min	333.51 (73.50)	304.51 (85.52)	.174	348.74 (61.89)	342.83 (56.64)	.655	.285	.050
Ratio (PSQI:actigraphy), %	74.55 (26.58)	77.82 (40.71)	.727	76.57 (21.53)	66.39 (22.20)	.034*	.687	.210
Sleep efficiency								
PSQI, %	68.17 (21.44)	59.55 (25.66)	.173	66.48 (20.52)	58.19 (18.36)	.059	.709	.819
Actigraphy, %	81.10 (8.59)	79.87 (9.12)	.601	83.07 (7.65)	79.57 (8.14)	.043*	.253	.900
Ratio (PSQI:actigraphy), %	85.66 (29.45)	76.86 (39.58)	.341	80.68 (26.44)	73.44 (22.39)	.193	.401	.699

Student's *t* test and Mann-Whitney *U* test were used for differences between means. Data are presented as mean (standard deviation). *$P < .05$. PSQI = Pittsburgh Sleep Quality Index, TIB = time in bed, TST = total sleep time. Sleep-log refers to the daily sleep diary accompanying actigraphy.

Figure 1—(A–D) Comparison of electroencephalographic spectral power between sex groups.



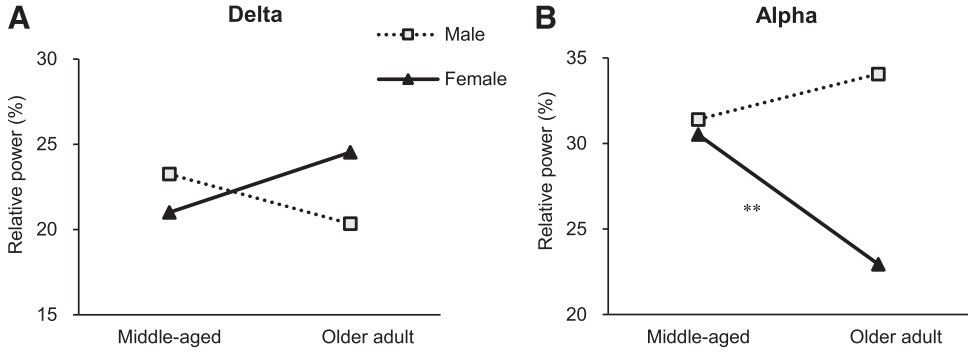
Vertical bars represent standard errors. *$P < .05$, **$P < .01$.

younger counterparts, was statistically significant in women ($P = .013$) but not in men ($P = .226$) in subgroup analyses.

DISCUSSION

This study investigated age, sex, and their interactive effects on clinical sleep parameters and resting-state quantitative EEG in patients with insomnia disorder. Women with insomnia had a longer sleep time by actigraph than men, and in the older adult group women stayed in bed for a longer time than men. Regarding age effects, older adults with insomnia generally had poorer sleep compared with middle-aged adults. Especially older women reported shorter perceived sleep time with more self-reported and objective discrepancy compared with their younger counterparts. In the quantitative EEG analysis, women had higher beta power than men, and DOF was slower in the older adult group compared with the middle-aged groups. In

Figure 2—Group by sex interaction effects on delta **(A)** and alpha **(B)** bands in the frontal area.



Relative alpha power in the frontal area was significantly lower in the female older adult group than in their younger counterparts. $^{**}P < .01$.

addition, interaction between age and sex was significant for frontal alpha and delta power, revealing different age effect on EEG activity in men and women.

First, this study examined the age and sex effects on insomnia. Our result of older patients having more disturbed sleep than middle-aged patients is in line with the previous studies in the general population. Older adults are known to have decreased TST and SE and increased WASO compared with younger adults.[1,27] Although the actigraphic results did not reach statistical significance, there was a trend of expected direction with older patients showing shorter TST, lower SE, and longer WASO than younger patients. Meanwhile, women reported their sleep to be as poor as men's sleep despite women's longer sleep time by actigraphy, which is similar to what is known in the general population that women self-report more impaired sleep while objective sleep is less fragmented and longer than in men.[1,28–30]

We failed to find a significant age by sex interaction on clinical parameters. Nevertheless, there were notable findings from subgroup analyses. Based on the findings that older patients showed more disturbed sleep and women tended to underestimate their sleep, older women might be the most susceptible group to insomnia. Older women with insomnia did show more impaired actigraphic SE and shorter PSQI TST compared with younger women. Interestingly, the ratio of TST was much lower in the older female group; PSQI sleep time reported by older women was 66.4% of their actigraphic sleep time, which was much less than the 76.6% reported by middle-aged women. Older females with insomnia might be particularly prone to interpret their sleep as poor. In addition, we found that older women with insomnia spent significantly more TIB than older men, with a mean TIB of 433 minutes for older women and 379 minutes for older men. Such lengthened TIB for older females might be an intentional attempt to restore sleep duration or a secondary consequence of sleep deprivation. This unique behavioral adaptation of older women might result from their greater awareness of insomnia symptoms or less tolerance of sleep deficit. Ironically, as TIB lengthens, not only TST, but also WASO, increases proportionately or disproportionately. An increased WASO accompanying a lengthened TIB may degrade sleep quality and cause more dissatisfaction of sleep regardless of the preserved total amount of sleep. Therefore, reducing TIB, one of the key pillars of cognitive-behavioral therapy for insomnia, might be particularly beneficial for older female patients with insomnia, who are more likely to have lengthened TIB.

In addition, the difference in brain activity in insomnia according to age and sex was investigated. In the present study, women with insomnia showed higher beta power in the whole brain area than men. Increased EEG power of high frequency has been taken as an indicator of cortical arousal in insomnia.[31] Furthermore, a positive correlation between heightened beta power and hyperarousal was reported.[23] Taken together, the finding that women showed higher beta power than men may suggest a predisposition to hyperarousal in women compared with men. This is consistent with a previous functional magnetic resonance imaging study in insomnia revealing more brain dysfunction areas in women than in men, which was interpreted in relation to stronger hyperarousal.[32]

Between the age groups, the DOF was significantly slower in the older adult group than in the middle-aged group. EEG slowing is known to be associated with aging and, more important, impaired working memory and cognitive performance.[33] It is usually observed in neurodegenerative disorders[34,35] but is also reported in various states of impaired cognition including cancer-related fatigue,[36] burnout syndrome,[37] and depression.[38] Patients with insomnia disorder may show an impaired working memory and executive function compared with good sleepers,[39] the degree of which correlates with the self-reported severity of insomnia symptoms.[40] The slower DOF in older patients with insomnia may reflect not only aging but also their more impaired sleep and, presumably, change in cognitive ability.

The interaction between age and sex on spectral EEG was found in the frontal area. Considering the role of the frontal lobe in sleep, emotional process, and cognition, it is noteworthy that the age effect on frontal activity differs between men and women with insomnia. The distinct frontal activity changes in older women with insomnia may hint at the possibility of their biological vulnerability related to their excessive distress from insomnia. In previous studies, reduced power of alpha and increased power of slow wave activity (ie, theta and delta) have

been repeatedly observed after sleep loss,[41–43] especially in the frontal region.[43–45] Although further study is needed to confirm whether frontal brain activity in insomnia is related to sleep loss, lower frontal alpha power in older women among patients with insomnia may represent their increased susceptibility to sleep loss. Several reports indicate that women are more biologically susceptible to sleep loss.[46,47] The increase in slow-wave sleep after sleep deprivation was more prominent in women than in men, suggesting that sleep debt might accumulate faster and require a more urgent response for recovery in women than in men.[46] Older women are also more likely to develop hypertension and have high cholesterol levels after sleep deprivation than men of the same age.[47] Our results further suggest that the susceptibility to sleep deficit in women may increase with age, according to the decreasing frontal alpha activity. This susceptibility may lead to more awareness of insomnia symptoms and/or less tolerance of sleep disturbance in older women, which may also underlie the higher prescription rate of sleep aids in older female patients.[9–11]

This study has several limitations. First, due to the cross-sectional design of this study, there were limitations in assessing the temporal link between clinical sleep parameters and quantitative EEG change. Second, multiple statistical comparisons without corrections were made. Caution is needed regarding the statistical significance and the interpretation of the results. Third, we compared between age groups and sexes among patients with insomnia without control patients. Therefore, we could not define whether the difference according to age or sex was physiologic or specific to insomnia. Finally, since disease duration was not determined, we could not clarify if the difference found between age groups was caused by an accumulating effect of longer disease duration.

CONCLUSIONS

Women with insomnia showed more excessive hyperarousal presented by elevated high-frequency power of waking EEG compared with men. The higher incidence of insomnia in women may be attributed to women's predisposition to hyperarousal, which may also explain their tendency to interpret their sleep as poor. An age-related difference in insomnia was observed as well in that older patients tended to have more sleep disturbance and a slower DOF. Older women appeared to be particularly distressed by insomnia, characterized by underrating their sleep time and increasing TIB. Clinicians should be aware of age and sex differences in insomnia, which may further impact behaviors of patients, such as staying in bed for a longer time and seeking sleep aids.

ABBREVIATIONS

DOF, dominant occipital frequency
EEG, electroencephalography
PSQI, Pittsburgh Sleep Quality Index
SE, sleep efficiency
TIB, time in bed
TST, total sleep time
WASO, wake after sleep onset

REFERENCES

1. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*. 2004;27(7):1255–1273.
2. Redline S, Kirchner HL, Quan SF, Gottlieb DJ, Kapur V, Newman A. The effects of age, sex, ethnicity, and sleep-disordered breathing on sleep architecture. *Arch Intern Med*. 2004;164(4):406–418.
3. Lindberg E, Janson C, Gislason T, Björnsson E, Hetta J, Boman G. Sleep disturbances in a young adult population: can gender differences be explained by differences in psychological status? *Sleep*. 1997;20(6):381–387.
4. Zhang B, Wing Y-K. Sex differences in insomnia: a meta-analysis. *Sleep*. 2006;29(1):85–93.
5. Singareddy R, Vgontzas AN, Fernandez-Mendoza J, et al. Risk factors for incident chronic insomnia: a general population prospective study. *Sleep Med*. 2012;13(4):346–353.
6. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev*. 2002;6(2):97–111.
7. Bin YS, Marshall NS, Glozier N. The burden of insomnia on individual function and healthcare consumption in Australia. *Aust N Z J Public Health*. 2012;36(5):462–468.
8. Li RH, Wing YK, Ho SC, Fong SY. Gender differences in insomnia—a study in the Hong Kong Chinese population. *J Psychosom Res*. 2002;53(1):601–609.
9. Chong Y, Fryar CD, Gu Q. Prescription sleep aid use among adults: United States, 2005-2010. *NCHS Data Brief*. 2013;(127):1–8.
10. Stewart R, Besset A, Bebbington P, et al. Insomnia comorbidity and impact and hypnotic use by age group in a national survey population aged 16 to 74 years. *Sleep*. 2006;29(11):1391–1397.
11. Chung S, Park B, Yi K, Lee J. Pattern of hypnotic drug prescription in South Korea: health insurance review and assessment service—national patients sample. *Sleep Med Res*. 2013;4(2):51–55.
12. Pillai V, Roth T, Drake CL. The nature of stable insomnia phenotypes. *Sleep*. 2015;38(1):127–138.
13. Jaussent I, Dauvilliers Y, Ancelin ML, et al. Insomnia symptoms in older adults: associated factors and gender differences. *Am J Geriatr Psychiatry*. 2011;19(1):88–97.
14. Riemann D, Spiegelhalder K, Feige B, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep Med Rev*. 2010;14(1):19–31.
15. Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. *J Sleep Res*. 1997;6(3):179–188.
16. Staner L, Cornette F, Maurice D, et al. Sleep microstructure around sleep onset differentiates major depressive insomnia from primary insomnia. *J Sleep Res*. 2003;12(4):319–330.
17. Lamarche CH, Ogilvie RD. Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. *Sleep*. 1997;20(9):726–733.
18. Perlis ML, Smith MT, Andrews PJ, Orff H, Giles DE. Beta/gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. *Sleep*. 2001;24(1):110–117.
19. Perlis ML, Kehr EL, Smith MT, Andrews PJ, Orff H, Giles DE. Temporal and stagewise distribution of high frequency EEG activity in patients with primary and secondary insomnia and in good sleeper controls. *J Sleep Res*. 2001;10(2):93–104.
20. Merica H, Blois R, Gaillard JM. Spectral characteristics of sleep EEG in chronic insomnia. *Eur J Neurosci*. 1998;10(5):1826–1834.
21. Buysse DJ, Germain A, Hall ML, et al. EEG spectral analysis in primary insomnia: NREM period effects and sex differences. *Sleep*. 2008;31(12):1673–1682.

22. Choi H, Jeong J, Kim H, Shin C, Yoon IY. Implication of fast activities of spectral analysis in subjective sleep complaints of elderly women. *J Geriatr Psychiatry Neurol*. 2019;32(1):24–30.
23. Wołyńczyk-Gmaj D, Szelenberger W. Waking EEG in primary insomnia. *Acta Neurobiol Exp (Warsz)*. 2011;71(3):387–392.
24. Kwan Y, Baek C, Chung S, Kim TH, Choi S. Resting-state quantitative EEG characteristics of insomniac patients with depression. *Int J Psychophysiol*. 2018; 124:26–32.
25. Vanable PA, Aikens JE, Tadimeti L, Caruana-Montaldo B, Mendelson WB. Sleep latency and duration estimates among sleep disorder patients: variability as a function of sleep disorder diagnosis, sleep history, and psychological characteristics. *Sleep*. 2000;23(1):71–79.
26. Zeger SL, Liang K-Y. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. 1986;42(1):121–130.
27. Yoon IY, Kripke DF, Youngstedt SD, Elliott JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res*. 2003;12(2): 87–93.
28. van den Berg JF, Miedema HM, Tulen JH, Hofman A, Neven AK, Tiemeier H. Sex differences in subjective and actigraphic sleep measures: a population-based study of elderly persons. *Sleep*. 2009;32(10):1367–1375.
29. Wauquier A, van Sweden B, Lagaay AM, Kemp B, Kamphuisen HA. Ambulatory monitoring of sleep-wakefulness patterns in healthy elderly males and females (greater than 88 years): the "Senieur" protocol. *J Am Geriatr Soc*. 1992;40(2): 109–114.
30. Sakakibara S, Kohsaka M, Kobayashi R, Honma H, Fukuda N, Koyama T. Gender differences in self-evaluated sleep quality and activity of middle-aged and aged subjects. *Psychiatry Clin Neurosci*. 1998;52(2):184–186.
31. Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. *Sleep Med Rev*. 2010;14(1):9–15.
32. Dai XJ, Nie X, Liu X, et al. Gender differences in regional brain activity in patients with chronic primary insomnia: evidence from a resting-state fMRI study. *J Clin Sleep Med*. 2016;12(3):363–374.
33. Klimesch W. α-band oscillations, attention, and controlled access to stored information. *Trends Cogn Sci*. 2012;16(12):606–617.
34. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res Brain Res Rev*. 1999;29(2-3): 169–195.
35. Garcés P, Vicente R, Wibral M, et al. Brain-wide slowing of spontaneous alpha rhythms in mild cognitive impairment. *Front Aging Neurosci*. 2013;5:100.
36. Zimmer P, Mierau A, Bloch W, et al. Post-chemotherapy cognitive impairment in patients with B-cell non-Hodgkin lymphoma: a first comprehensive approach to determine cognitive impairments after treatment with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone or rituximab and bendamustine. *Leuk Lymphoma*. 2015;56(2):347–352.
37. van Luijtelaar G, Verbraak M, van den Bunt M, Keijsers G, Arns M. EEG findings in burnout patients. *J Neuropsychiatry Clin Neurosci*. 2010;22(2):208–217.
38. Tement S, Pahor A, Jaušovec N. EEG alpha frequency correlates of burnout and depression: the role of gender. *Biol Psychol*. 2016;114:1–12.
39. Fortier-Brochu E, Beaulieu-Bonneau S, Ivers H, Morin CM. Insomnia and daytime cognitive performance: a meta-analysis. *Sleep Med Rev*. 2012;16(1): 83–94.
40. Szelenberger W, Niemcewicz S. Severity of insomnia correlates with cognitive impairment. *Acta Neurobiol Exp (Warsz)*. 2000;60(3):373–376.
41. Ferreira C, Deslandes A, Moraes H, et al. Electroencephalographic changes after one night of sleep deprivation. *Arq Neuropsiquiatr*. 2006;64(2b):388–393.
42. Cote KA, Milner CE, Smith BA, et al. CNS arousal and neurobehavioral performance in a short-term sleep restriction paradigm. *J Sleep Res*. 2009;18(3): 291–303.
43. Corsi-Cabrera M, Sánchez AI, del-Río-Portilla Y, Villanueva Y, Pérez-Garci E. Effect of 38 h of total sleep deprivation on the waking EEG in women: sex differences. *Int J Psychophysiol*. 2003;50(3):213–224.
44. Cajochen C, Foy R, Dijk D-J. Frontal predominance of a relative increase in sleep delta and theta EEG activity after sleep loss in humans. *Sleep Res Online*. 1999;2(3):65–69.
45. Forest G, Godbout R. Effects of sleep deprivation on performance and EEG spectral analysis in young adults. *Brain Cogn*. 2000;43(1-3):195–200.
46. Armitage R, Hoffmann RF. Sleep EEG, depression and gender. *Sleep Med Rev*. 2001;5(3):237–246.
47. Aldabal L, Bahammam AS. Metabolic, endocrine, and immune consequences of sleep deprivation. *Open Respir Med J*. 2011;5(1):31–43.

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DISCLOSURE STATEMENT

All authors have read and approved the manuscript. Work for this study was performed at Seoul National University Bundang Hospital. The authors report no conflicts of interest.